The private pharmaceutical industry and its impact on health

Nuria Homedes December 2017

The pharmaceutical industry

- Maximize income: increasing the volume of sales and prices
- Health professionals: maximize benefits for patients and the population



Outline

- Some characteristics of the global pharmaceutical industry
- Current problems with access and appropriate use
- How does the industry contribute to access and appropriate use of pharmaceuticals
- What is the role of the FDA and other regulatory agencies
- What can be done?

Characteristics of the pharmaceutical market

Consolidation of the industry

- In 1987 the top 10 manufacturers had 27.5% of the world's pharmaceutical market
 - By 2000 the percentage increased to 42%
 - By 2007, ten companies controlled 46% of the market
 - Since then we have seen some decline (biologics?)

Declining Market Share of Big Pharma

Market Share of Top 10 Pharmaceutical Companies



www.revenuesandprofits.com



The market share of biopharmaceuticals is growing but is controlled by only a few key companies



2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011



Average profit margins of five main industrial sectors, 2013



Note: Highest/lowest profit margins achieved by an individual company Source: Forbes

http://www.saludyfarmacos.org/boletin-farmacos/boletines/nov2014/p44758

World's largest pharmaceutical firms								
Company	Total revenue (\$bn)	R&D spend (\$bn)	Sales and marketing spend(\$bn)	Profit (\$bn)	Profit margin (%)			
Johnson & Johnson (US)	71.3	8.2	17.5	13.8	19			
Novartis (Swiss)	58.8	9.9	14.6	9.2	16			
Pfizer (US)	51.6	6.6	11.4	22.0	43			
Hoffmann-La Roche (Swiss)	50.3	9.3	9.0	12.0	24			
Sanofi (France)	44.4	6.3	9.1	8.5	11			
Merck (US)	44.0	7.5	9.5	4.4	10			
GSK (UK)	41.4	5.3	9.9	8.5	21			
AstraZeneca (UK)	25.7	4.3	7.3	2.6	10			
Eli Lilly (US)	23.1	5.5	5.7	4.7	20			
AbbVie (US)	18.8	2.9	4.3	4.1	22			
Source: GlobalData								

Richard Anderson. Pharmaceutical industry gets high on fat profits

BBC News, 6 November 2014 http://www.bbc.com/news/business-28212223

Access to pharmaceuticals

80% of medicines are 5.65% Asia consumed by 17% of the 7.75% population Africa 60.67% 10.82% 6.58E-5% **Breakdown of the World pharmaceutical market** USCB 2012 sales North America (USA & Canada) Europe 26.7% 41.0% Japan 11.7% 14.7% 5.9% Latin America Africa, Asia & Australia (Excluding Japan)

World Population By Continent

Antarctica

North America

South America Oceania

Europe

14.57%

0.53%

Access to medicines

- 1/3 of the population does not have access to essential medicines (20 medicines to treat priority health problems)
- According to HAI a selected list of generic medicines, that varies per country are available in

	Low income countries	Middle income countries
Public facilities	37.7%	46.0%
Private facilities	70.0%	71.7%

Haiweb.org/medicineprices (2012)

Access to medicines

- Per capita consumption:
 - US\$8 person/year in low income countries (2010)
 - US\$463.6 person/year in high income countries (2010)
- Private out-of-pocket expenditures have been rising in all countries, except high income, since 1995

☐ pharmaceutical prices have greatest impact on the poor and uninsured

Composition of per capita total pharmaceutical expenditure by income group, 2006 (in US\$ at exchange rate values)

	Total pharmaceutical expenditure						Total expenditure on health			
Income		Public		Private		Total	Public	Private	Total	
group	Ν	US\$	%	US\$	%	US\$	US\$	US\$	US\$	N
High	42	264.4	61.3	167.2	38.7	431.6	2473.6	1597.6	4071.4	49
Upper middle	31	32.6	38.8	51.5	61.2	84.1	214.7	184.1	398.8	54
Lower middle	34	10.5	33.5	20.8	66.5	31.3	27.5	38.6	66.1	47
Low	27	1.76	23.1	5.85	76.9	7.61	19.2	3.7	22.9	41

Table 4.1.5: Total Pharmaceutical Expenditures (2010)

	Population		Total Pharmaceutical Expenditure							
Country group (number of countries)	Millions	%	Million US\$	%	%THE	%GDP	Per capita (US\$)			
WHO region										
Africa (43)	819	12.1%	\$19,464	1.7%	23.0%	1.3%	\$10.59			
Americas (35)	923	13.6%	\$436,004	38.7%	19.8%	1.3%	\$87.30			
Eastern Mediterranean (19)	573	8.4%	\$20,763	1.8%	20.1%	1.2%	\$50.31			
Europe (52)	896	13.2%	\$331,683	29.5%	21.5%	1.6%	\$308.48			
South-East Asia (10)	1,783	26.2%	\$41,157	3.5%	33.2%	1.3%	\$13.05			
Western Pacific (27)	1,800	26.5%	\$276,362	24.6%	18.7%	1.2%	\$37.90			
World Bank income grou	р									
High-income (49)	1,092	16.1%	\$775,305	68.9%	18.5%	1.4%	\$463.59			
Upper-middle-income (55)	2,474	36.4%	\$283,864	25.2%	21.2%	1.3%	\$96.78			
Lower-middle-income (50)	2,480	36.5%	\$59,580	5.3%	23.6%	1.3%	\$26.28			
Low-income (32) Global	749	11.0%	\$6,683	0.6%	27.7%	1.6%	\$8.01			
Global (186)	6,795		\$1,125,433		20.8%	1.4%	\$68.78			

Source: World Health Organization Global Health Observatory Database, 2013 National Health Accounts, 2013



Financing: Share of Total Pharmaceutical Expenditure (TPE) in Total Health Expenditure (THE) and Gross Domestic Product (GDP), 2010

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Source: National Health Accounts 2010 (http://www.who.int/nha/en)

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Treatment affordability for adult respiratory infection (expressed as the number of days the lowest-paid government worker needs to work to pay for a 7-day course of treatment with ciprofloxacin, 500 mg twice daily)



* Affordability is calculated as 0.1 day's wages.

^b Results of a sub-national survey conducted in Gauteng Province.

Source: Based on results of surveys of medicine prices and availability conducted using the WHO/HAI standard methodology and collated by HAI (http://www.haiweb.org/medicineprices/).



Where multiple state or provincial surveys have been conducted (i.e. India, Sudan), results from individual surveys have been averaged without weighting.

Source: Based on results of surveys of medicine prices and availability conducted using the WHO/HAI standard methodology and collated by HAI (http://www.haiweb.org/medicineprices/).

Exhibit 6

Adults Who Cited Cost as a Reason for Skipping Prescriptions or Doses, 2016



s://infogram.com/5a9fddb9-0f27-4261-a2bc-88a83705822f

The rising cost of new pharmaceuticals

- 11 of the 12 cancer products approved by the FDA in 2012 cost more than US\$100.000 per treatment
- 15 cancer drugs introduced in the past 5 years cost more than \$10,000 a month
- A cholesterol-lowering treatment for those with certain rare genetic disorders costs \$311,000 a year
- A cystic fibrosis medicine—developed partly with funding from a charity—costs \$300,000 annually

Rising prices of existing drugs

- Since December 2014 until February 2016, out of 3,000 brand-name prescription: 60 doubled in price and 20 quadrupled it
- The price of Alcortin A soared 1,860 percent, or almost 20fold
- In past two months (up to 2/2016): Pfizer raised prices for 24 drugs by at least 12% and GlaxoSmithKline increased prices for 22 products by 15 %
- Even prices for some brand drugs that have long lost patent protection are rising sharply. AstraZeneca sold U.S. rights to two old blood pressure drugs, Zestril and Tenormin, to Alvogen in January 2015. Alvogen has raised the prices for Zestril by about 800 % and Tenormin by about 600%

Rising prices of existing pharmaceuticals

Costly Care

The price of many top-selling prescription medicines has increased steadily over the past seven years



GRAPHIC BY BLOOMBERG BUSINESSWEEK. SOURCE: DRX, DATA COMPILED BY BLOOMBERG

The consumer price index rose just 12 percent during the period

Prices Soar for an Old Antidepressant

Valeant has raised Wellbutrin XL's price 11 times since early 2014, despite generic competitors.



Source: SSR Health Note: Prices are list price for 30 tablets of Wellbutrin XL, 300 mg dose.

Bloomberg 💵

GRAPH 1: THE RISING PRICE OF IMMUNISING A CHILD

Estimated cost to purchase a full course of vaccines according to WHO Recommended Routine Immunisation Schedule



Timeline: WHO recommendations & vaccine introduction

2001: Baseline vaccine package includes 1BCG, 3 oral polio vaccine (OPV), 3 DTP and 2 measles.

2004: WHO reiterates 1992 recommendation for universal vaccination against Hepatitis B.

2006: WHO recommends universal vaccination against Haemophilus influenzae type B.

2010: First GAVI-eligible country receives pneumoccocal conjugate vaccine under the Advance Market Commitment (WHO recommended vaccination with PCV in 2007).

2011: First GAVI-eligible country in Africa receives rotavirus vaccine (WHO recommended vaccination with rotavirus vaccine in 2009). WHO recommends universal immunisation with rubella vaccine and GAVI Board endorses decision to open a rubella vaccine funding window. Appropriate use of pharmaceuticals

Access vs Appropriate Use

- Appropriate use of medicines requires the correct:
 - Diagnosis, prescription and dispensation of medicines: adequate dosages, correct time interval between dosages, for an adequate duration, at the lowest cost to them and their community
- Less than 50% of the medicines are appropriately prescribed and dispensed; and only 50% of the patients take their medicines according to the prescriber's advice

Inappropriate use of pharmaceuticals

- New prescription drugs have a 1 in 5 chance of causing serious reactions (7 year rule)
- Properly prescribed drugs (aside from misprescribing, overdosing, or self-prescribing) cause about 1.9 million hospitalizations per year
- Another 840,000 hospitalized patients are given drugs that cause serious adverse reactions for a total of 2.74 million serious adverse drug reactions per year
- About 128.000 people in the USA and 200.000 in Europe die as a result of pharmaceutical consumption
- At least 1.5 million preventable adverse drug events every year, with costs exceeding \$4 billion annually
- Drug-related morbidity and mortality estimated to cost \$177 billion per year (2000), with hospital admissions accounting for 70% of the cost
- Prescription drugs are the 4th cause of death (with stroke) some say the 3rd

Medication cycle: stages and actors



How does the pharmaceutical industry affect access and appropriate use of pharmaceuticals

How?

- Deciding what to research
- Increasing the demand for medicines through promotion (prescribers, dispensers, community, including academic literature)
- Influencing formularies of pharmaceutical payers
- Educating prescribers on how to prescribe and consumer what they want (may or not need): promotion
- Deciding where to market the medicines only where they will be purchased at the price that they want to sell
- Influencing government and regulatory agencies so that they adopt policies that benefit the industry: trade agreements, lobbying, revolving doors

Research priorities

- Medicines for those who can afford to pay. Only 10% of research funds are allocated to the priorities of developing countries, where >85% of the population lives.
- Limited research for 5000+ rare diseases
- Industry only invests if they can sell 250 million a year during 14 years
- Recently a few initiatives have been established with public funds and philanthropy to do research for rare and neglected diseases

New antibacterial molecular entities approved by the FDA 1983-2002



How do they decide what new medicines to research

- Fill a void in therapeutic options (should be but mainly they invest in me too drugs, because there is a market [] new drugs more expensive than old drugs)
- Gain market share
- Increase return on investment (invest in R&Dpay investors – marketing (gifts to prescribers, CMEs, subscriptions, conferences– large compensation packages – fines- donations)

Innovation

- There are very few truly new innovative drugs commercialized every year (about 30 NME, but only 1-2 are true innovation).
- According with the Office of Technology Assessment (USA), 97% the products approved by the FDA during the last 25 years were *mee too* drugs (more expensive but adding little therapeutic value). 70% of the 3% of useful medicines had been discovered in public laboratories.
- The research units are difficult to merge [] less innovation (although some disagree)

New Drugs, 2002-2011 918



Increasing demand for medicines

- Medicalizing life: behavioral problems have been transformed into new diseases (ADHD, social anxiety disorder, premenstrual dysforic disorder, and gastroesophageal reflux).
- Lifestyle drugs: to control obesity, male baldness, to enhance the erectile function in healthy young men and low sexual desire in premenopausal women...
- Changes in disease definition: Often members of panels to decide on disease definition or treatment protocols have conflicts with the industry (8 of 9 who decided to lower recommended levels of cholesterol [] an increase in yearly sales of drugs of 40 million; and 9/11 who changed the definition of HBP)

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Source: GlobalData					

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BBC News, 6 November 2014 http://www.bbc.com/news/business-28212223

HOW MUCH DOES BIG PHARMA SPEND ON: SALES & MARKETING VS. RESEARCH & DEVELOPMENT



https://www.washingtonpost.com/news/wonk/wp/2015/02/11/big-pharmaceuticalcompanies-are-spending-far-more-on-marketing-than-research/

Global Overview

INVESTMENT BY CHANNEL FULL YEAR 2014





Total All Channels



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Deciding where to sell: Recent Study

- 33 NME approved by the FDA in 2011 and 2012 had been tested in Latin America (pivotal trials)
- Two years later:
 - Eight products were registered and commercialized in all the countries where tested
 - Ten products were not registered or commercialized in any of the countries where tested
 - Only 51% of the products were available where tested
 - 36.4% of the products were not marketed in any of the countries where they were tested
- The industry's decision to conduct the trial is independent from its intention to register and commercialize the product

Affordability of NME

- We obtained prices for 18 of the 21 products marketed in LA, and they varied widely across countries
- A course of treatment with these 18 products, except 1, cost more than one monthly minimum wage (MMW). Five cost 1-4 times the MMW, while six cost 100-896 MMW. The exception is rivoraxavan for hip and knee replacements

Added value of NME

- Independent drug bulletins had evaluated 25 of the 33 NME
- 20 of the 25 were inferior to existing treatments
- 5 could offer some benefits to a specific group of patients with significant side-effects*

The role of government and the regulatory agencies

What's the role of the FDA?

- Established in 1906 regulates food, medical devices and pharmaceuticals
- The Center for Drug Evaluation and Research (CDER)
 - Approves drugs based on safety (since 1938) and efficacy (since 1962)
 - Determines over-the-counter vs. prescription status
 - Approves product label written by producer
 - Monitors possible medication side effects through adverse event reporting (voluntary for MDs and consumers, mandatory for industry) [] recommends changes to label or withdrawals from the market

The FDA does not:

- Determine optimal therapy for a condition
- Test drugs—it relies on data submitted by the drug sponsor, it only inspects 2% of the clinical trial sites – mainly in high income countries. Does not control the actual implementation of the trial
- Refuse approval for a drug just because there are similar drugs on the market
- Make approval decisions based on the economic impact of a drug for patients or insurers
- Pre-approve marketing materials (have to be based on information in label)
- Control the price of pharmaceuticals

The problem

- The FDA is mostly funded by Congress, but about half the budget for drug evaluations is paid by the pharmaceutical industry
 - The Prescription Drug User Fee Act (PDUFA) was passed in 1992
 - PDUFA provides funding of FDA regulatory activities by those being regulated and sets out the time constraints under which the FDA must complete its review of an NDA

Weaknesses in the system

- Pharmaceutical companies put pressure on Congress and the FDA to:
 - accelerate the approval of medicines [] each extra day in the market can represent millions of dollars on sales (for blockbusters it has been estimated about US\$6 million per day)
 - Maintain high prices: no price regulation (only for Veterans Administration), trade agreements, delaying generic competition
- The entire commercialization process (from the design of the clinical trial to the analysis of the data is on the hands of the manufacturers)



Weaknesses in the system (2)

- There is very little oversight on the quality of the data obtained during the clinical trials and of the data analysis
- Concerns have been raised about the manipulation of clinical trial results to disguise side effects (Vioxx is a well known example but there are many others - antidepressants)
- Increasing concern about inappropriate marketing of drugs (multi-billion fines paid by industry every year) [] higher prices

Weaknesses in the system (3)

- There is a tendency to decrease the recommendation of market withdrawals (instead black-box warnings are included in the label)
- Fines for fraud in billing, advertising, collusion are increasing but the amounts do not discourage the industry from engaging in unethical/unlawful behaviors
- The industry has developed excellent marketing strategies and is the main supplier of pharmaceutical information for health professionals and community at large

Summary

- The FDA and other regulatory agencies face difficulties controlling the R & D, production and marketing of pharmaceuticals
- Governments, insurance companies and patients are held hostage to the prices imposed by Pharma companies [] mergers increase their monopoly power (this also affects generic producers)
- Double burden: excessive consumption by some and insufficient access by others (low income, uninsured and poor in US, affected by rare diseases)

Suggestions

- De-link the cost of research and development of new medicines from price [] establish competitive manufacturing systems to bring down prices
- Funding of regulatory agencies independent of the industries they regulate
- Increase public access to PhARMA and FDA data
- Increase oversight of clinical research and find mechanisms to double-check industry reports

Suggestions

- Educate communities, patients, health professionals on the need to use medicines appropriately
- Delink the continuing education of health professionals (and students) from industry
- Price controls
- Control/eliminate conflicts of interest between drug manufacturers – health professionals – patients' groups

Questions?